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Implantable arterial port-related bloodstream infection in patients with primary or metastatic hepatic malignancies

Hitoshi Honda, MD[1], **Yasuo Sakurai, MD**[2], **Jong-Hon Kang, MD**[3], **Tadahiro Nakamura, MD**[1], **Hirotaka Matsuura, MD**[1], and **David K Warren, MD, MPH**[4]

[1]Department of General Internal Medicine and Infectious Diseases, Teine, Keijinkai Medical Center, Sapporo, Japan

[2]Department of Radiology, Teine Keijinkai Medical Center, Sapporo, Japan

[3]Center for Gastroenterology, Teine Keijinkai Medical Center, Sapporo, Japan

[4]Division of Infectious Diseases, Department of Internal Medicine, Washington, University School of Medicine, St, Louis, USA

Abstract

The incidence of implantable arterial post-related bloodstream infections (IAP-RBSI) among patients with unresectable hepatic malignancies is not well defined. We reviewed the 9-year incidence of IAP-RBSI in patients with hepatic malignancies, at a tertiary care center in Japan. The incidence was 1.9 infections per 10,000 catheter days.

Hepatic malignancies including primary (i.e., hepatocellular carcinoma; HCC) and metastatic tumors cause substantial mortality. Although intra-hepatic infusion of chemotherapeutic agents via an implanted arterial port has been used for treating unresectable HCC or hepatic metastases,[1–3] the incidence of implantable arterial port-related bloodstream infections (IAP-RBSI) has not been previously examined. We reviewed the incidence of IAP-RBSI in patients with hepatic malignancies.

Methods

A retrospective cohort study was conducted from January 2003 through December 2011 at Teine Keijinkai Medical Center, a 551-bed, tertiary care center in Sapporo, Japan. Patients with hepatic malignancies, who had an implantable arterial port placed for intra-arterial infusion were eligible. Patients were excluded if they received an implantable arterial port

Corresponding author: Hitoshi Honda MD., Department of General Internal Medicine and Infectious Diseases, Teine Keijinkai Medical Center, 12-1-40 Maeda 1 jo Teine-ku, Sapporo, Hokkaido, 006-8555, JAPAN, Tel: 81-11-681-8111. Fax: 81-11-685-2196, hondah@hotmail.com. **Alternate corresponding author:** David Warren MD, MPH, Division of Infectious Diseases, Department of Internal Medicine, Washington, University School of Medicine, St, Louis, USA., 660 S. Euclid Ave. Campus Box 8051 Saint Louis, MO 63110-1093, Telephone: 314-454-8354 Fax: 314-454-5392, dwarren@dom.wustl.edu.

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Potential conflicts of interest

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without receiving intra-arterial infusion at the study institution, or died before receiving intra-arterial infusion.

The catheter was inserted through the femoral artery and the tip of catheter was positioned in the proper hepatic artery under fluoroscopic guidance. The proximal end of catheter was then connected to the injection port (Cell Site®, Toray Medical Co., Tokyo, Japan), which was implanted subcutaneously in the thigh. Interventional radiologists adhered to maximal barrier precautions during the procedure. All patients received one dose of prophylactic antibiotic (cefazolin or cefmetazole) before the procedure.

Chemotherapeutic agents were administered via the implantable arterial ports and treatment cycles were repeated every 1 to 4 weeks, depending on patient's underlying malignancy. Intra-arterial infusion of chemotherapy was performed either in the hospital or at an outpatient clinic. Implantable arterial ports were flushed with heparin after each infusion and every two weeks.

The Center for Disease Control and Prevention-National Healthcare Safety Network (NHSN) definitions for the catheter-related bloodstream infection was adapted to define IAP-RBSI[4]; patient had clinical evidence of infection and at least one positive blood culture with organisms not related to an infection at another site. All blood cultures were drawn from peripheral vein, but not from implantable arterial ports. If central venous catheters were present at the time of the bloodstream infection, then this was not regarded as an IAP-RBSI, given the possibility of venous catheter-related bloodstream infection.

The incidence for IAP-RBSI was calculated as the number of cases per 10,000 catheter-days, per chemotherapy session (i.e., the number of administration of chemotherapeutic agents), and per catheter placement. Catheter-days were defined as the number of days between implantable arterial port placement and either the date of port removal, date of death, date of last follow up, or the study end date.[5] This study was approved by the Teine Keijinkai Medical Center Institutional Review Board.

Results

During a 9-year study period, 103 patients received implantable arterial ports. Six patients (5.8%) received infusion at different institutions, and two (1.9%) died before receiving an infusion, leaving 95 patients for analysis (Table 1). Five patients underwent a second implantable arterial port placement after the first port was removed because of complications; two had IAP-RBSI, three developed non-infectious complications. Therefore, 100 implantable arterial ports were placed (37,147 catheter-days; 2,622 chemotherapy sessions)

The median number of device-days for 100 catheters in 95 patients was 266 (range 13–1786). Twelve patients had positive blood cultures in the cohort. One patient had a central venous catheter in place and four had secondary bacteremia, leaving seven patients (7.4%) with IAP-RBSI (Table 2). The overall incidence of IAP-RBSI was 1.9 infections per 10,000 catheter-days (alternatively, 0.3 infections per 100 chemotherapy sessions or 7.0% of catheters placed). The incidence of IAP-RBSI was higher in the latter half of the study

period. (0.4 versus 6.3 infections per 10,000 catheter-days; incidence ratio, 17.3; 95% confidence interval, 3.4–88.6). The median time to IAP-RBSI was 74 days (range 13–633). Three (42.9%) patients did not have their catheter removed; one patient died within 11 days of diagnosis, one died 42 days after diagnosis, and the other died from recurrent bacteremia due to the same organism 119 days after diagnosis.

Eleven patients developed other infections after implantable arterial port placement. These included an arterial port pocket infection (n=1), bloodstream infection with a concomitant central venous catheter (n=1), empyema (n=1) and liver abscess/biloma (n=8).

Discussion

Very few studies have investigated the incidence of IAP-RBSI. A previous study reported 3 infections of the port chamber among 41 patients during 260 treatment courses, but details of the infections were not noted.[6] As the incidence of hepatic malignancies increases in the United States,[7, 8] intra-arterial infusion of chemotherapy becomes a more common treatment option.[1–3]

We found that IAP-RBSI occurred relatively infrequently and the incidence density was similar to that of implantable venous port-related bloodstream infections.[9] In our study, we determined IAP-RBSI incidence using three different denominators since a consensus to define the denominator for implantable ports was not completely established. Even though the NHSN definition states that ports are a permanent catheter and “device-days” should be used for denominator,[10] the frequency with which these catheters are accessed may be highly variable, depending on the patient’s chemotherapy course. This may lead to different risks for infection between patients. This challenge has led to using various definitions of catheter-days to assess venous port-related bloodstream infection in previous studies.[5, 9]

It remains unclear why the incidence of IAP-RBSI was higher in the latter half of the study period. There were differences in patient characteristics between the two periods, including hypertension and HCC, which were more common in the latter half of the study (data not shown). These changes might influence the observed difference in the incidence of IAP-RBSI.

The three patients who had attempted catheter salvage had unfavorable outcomes. Current guideline recommends the removal of implantable catheter for bloodstream infection, particularly due to *Staphylococcus aureus* and Gram-negative bacilli.[11]

In our study, we did not count as an IAP-RBSI in patients who developed liver abscess or biloma with bacteremia, as this have been a result of secondary infection of the hepatic tumor after chemotherapy. This, however, may have potentially led to an underestimation of IAP-RBSI incidence.

The current study demonstrated the incidence and microbiology of IAP-RBSI. Establishment of clear definition for a denominator to calculate incidence density for port catheters is warranted to assess port-related bloodstream infection.

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Table1

Demographic characteristics of 95 patients with an implantable arterial port placement for primary or metastatic hepatic malignancies.

Variable	n (%)
Age, year, median (range)	62 (41–81)
Male gender	71 (75)
Type of hepatic malignancy	
Hepatocellular carcinoma	64 (67)
Metastatic liver tumor[a]	31 (33)
Viral hepatitis	
None	46 (48)
Hepatitis B	22 (23)
Hepatitis C	26 (27)
Both hepatitis B and C	1 (1)
Child-Pugh classification at the time of an IAP placement	
Child-Pugh A	61 (64)
Child-Pugh B	31 (33)
Child-Pugh C	3 (3)
Diabetes mellitus	23 (24)
Alcohol use	35 (37)
Body mass index ≥ 25 kg/m^2	25 (26)

NOTE. IAP; implantable arterial port.

[a]Metastatic liver tumor included; colorectal cancer (n=18), cholangiocarcinoma (n=3), pancreatic cancer (n=2), breast cancer (n=1), and other cancer (n=7).

Table 2

Clinical and Microbiological Characteristics for Patients with Implantable Arterial Port-Related Bloodstream Infection

Case number	Age & gender	Underlying malignancy	Pathogens	Year of IAP placement	Time to IAP-RBSI (days)	Catheter removal	Outcome[a]	Antimicrobial therapy
1	55 y/o M	HCC	MSSA	2011	81	Yes	Cured	Cefazolin for 6 weeks
2	76 y/o F	HCC	MRSA	2010	60	Yes	Cured	Vancomycin for 4 weeks
3	54 y/o F	HCC	CoNS	2010	375	No	Died	Vancomycin/died within 11days during treatment
4	49 y/o M	HCC	*E.coli*	2009	50	No	Died	Ciprofloxacin for 3 weeks/developed recurrent bacteremia in 119 days
5	49 y/o F	HCC	MRSA	2009	66	Yes	Cured	Vancomycin for 2 weeks
6	66 y/o M	HCC	*E.coli*	2008	633	Yes	Cured	Ampicillin/sulbactam for 2 weeks
7	67 y/o M	HCC	*S. agalactiae*	2006	507	No	Died[b]	Cefepime for 2 weeks and died in 42 days

NOTE. IAP; implantable arterial port, IAP-RBSI; implantable arterial port-related bloodstream infection, M; male, F; female, HCC; hepatocellular carcinoma, MSSA; methicillin-susceptible *Staphylococcus aureus*, MRSA; methicillin-resistant *S. aureus*, CoNS; coagulase negative staphylococci, *E.coli; Escherichia coli*, *S. Agalactiae; streptococcus agalactiae*

[a] Implantable arterial port-related bloodstream infection were considered to be associated with an attributable mortality for all patients who died with the diagnosis of implantable arterial port-related bloodstream infection based on clinical information.

[b] Case 7 was transferred to a hospice care facility after 2 weeks treatment of antimicrobial therapy because of clinical deterioration.